Memorandu

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Biologics Evaluation and Research

Date: June 21, 2001

From: Carolyn Renshaw, HFM 675

Subject: Sanofi-Synthelabo Inc.
STN 103946/0
2/27/01 response to CR letter
Manufacture of Rasburicase for treatment of hyperuricemia

To: Gibbes Johnson, DTP
Sharon Sickafuse, DARP
John Finkbohner, DMPQ

I joined the review committee on 5/9/01 as a replacement for Patricia Hughes. I reviewed the responses to questions 10-24 contained in Volume 1 of Sanofi-Synthelabo Inc.'s 2/27/01 response to CBER's CR letter and I have the following comments:

Question 10 Response

- P.337 (Revised V.1.10/p.140): Please explain why the [redacted] test filter clogged during [redacted] testing and the possible effect of the clogging on the interpretation of the validation results.
- P.339 (Revised V.1.10/p.142): Sanofi states that the total worst case extractable substances expected is less than [redacted] mg in [redacted] L of bulk. I defer to the product reviewers to determine if this is acceptable.

Question 21 Response

P.155: I would like to discuss this response with the committee. If an [redacted] approach was used to validate the autoclave sterilization cycle, then Sanofi's statement that the [redacted] approach provides an appropriate level of sterility assurance even though the validation conditions were almost identical to the operating conditions [redacted]
Does the committee agree?

[redacted]

(I did not review the original application, therefore these questions may be irrelevant.)
Does the firm perform [redacted] testing of the in-process product after significant purification steps? Do they perform [redacted] testing of the final bulk?

cc:
Thomas HFM-675